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# MAGNETIC METHOD FOR DNA DETECTION ON AN ARRAYED SOLID STATE DEVICE

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**Abstract**

A unique solid-state giant magnetoresistive (GMR) biosensor is the centerpiece of an integrated sample processing system for the detection of target DNA molecules through hybridization. In addition to the electromagnetic instrumentation, surface chemistries and assays have been developed, as well as a cartridge-based microfluidics network in which pumps and valves are operated by an independent actuation mechanism.

**Keywords: Biosensor, DNA, fluidics, GMR, magnetic labeling**

## 1. Introduction

Current DNA array technologies often rely primarily on optical detection methods such as chemiluminescence, fluorescence, and colorimetric assays [1]. We have developed a fundamentally different technique to quantitatively detect and identify biological molecules. Our technique is based on the labeling of DNA molecules with magnetic microbeads and their subsequent detection with giant magnetoresistance (GMR) magnetic field sensors [2,3]. A complete analytical system called the Bead ARray Counter (BARC), which includes electronic instrumentation and fluidics, is being built around this technology. The fluidics component is essential to the efficiency at which the analytical instrument operates and the samples are analyzed. In addition, a successful early detection system suitable for field use requires components that are rugged and easy to use. It seems clear that in the interests of cost, construction, and maintenance, many microfluidics devices should be based on polymeric materials utilizing a minimal number of inexpensive parts [4]. We also feel that these same objectives can be further met by a synergistic design that couples disposable microfluidic components (e.g. pumps and valves) with reusable actuator devices. Our recent progress toward completion of the BARC system is described here.

## 2. Instrumentation

Over the last few years, BARC has witnessed an evolution in GMR sensor chip design. The most recent chip, BARC III, incorporates an array of 64 GMR sensors that show promise for improved detection efficiency and parallel analysis of multi-analyte DNA samples (Figure 1). Miniature fluidic devices and actuators have also been developed to automate the assay procedures. Microchannels, valve-less pumps, and

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pinch-valves have been cast into a polydimethylsiloxane (PDMS) membrane and packaged into a palm-sized cartridge along with the BARC sensor chip (Figure 2). Operation of the pumps and valves occurs when the cartridge is inserted into the BARC instrument and is mechanically coupled to an independent actuator block.

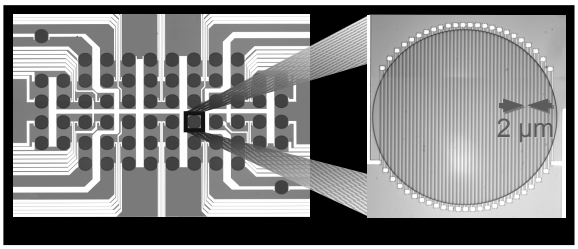


**Figure 1.** Micrograph showing the 64-sensor array on the BARC III chip. Each 200 µm-diameter sensor spot includes a single serpentine 2 µm-wide GMR sensor strip. A 0.2 µm-thick layer of $Si_3N_4$ protects the chip from the aqueous assay environment.

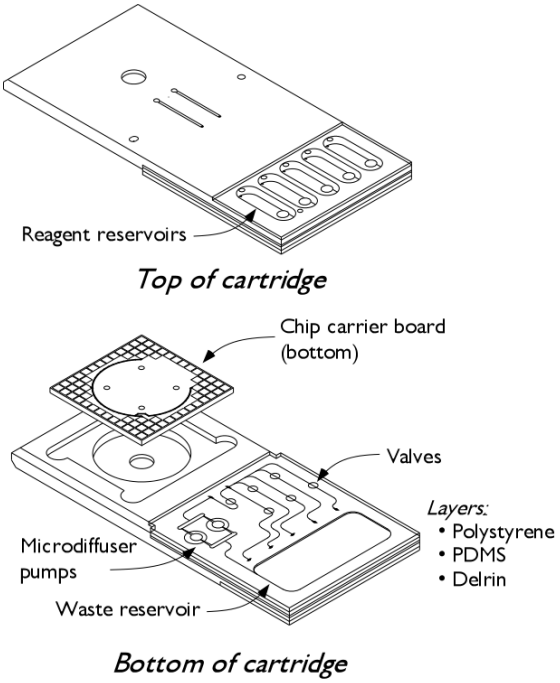


**Figure 2.** Schematic drawing of a 5.1 cm x 10.2 cm cartridge used to hold a PCB mounted BARC chip and a PDMS membrane containing a network of 125 µm-deep channels, valves, pumps and reservoirs. The cartridge interfaces with an independent pump and valve actuator block for automated dispensing of fluids.

## 3. Experimental assays

Distinct single-stranded DNA capture probes are immobilized on each sensor through thiol-gold chemistry. Sample target DNA, complementary to the immobilized probes, is allowed to hybridize on the chip followed by labeling with magnetic microbeads. The microbeads are then subjected to a magnetic field and detected by the GMR sensors.

Refinement of our hybridization and labeling methods has improved the overall sensitivity to 10 fM for a 15-minute hybridization time with 30 bp oligonucleotides (Figure 3). Further efforts to improve the sensitivity are currently underway; for example, we have been experimenting with peptide nucleic acid (PNA) capture and detection probes. Initial results with PNA indicate that an increase in sensitivity of one to two orders of magnitude can be expected.

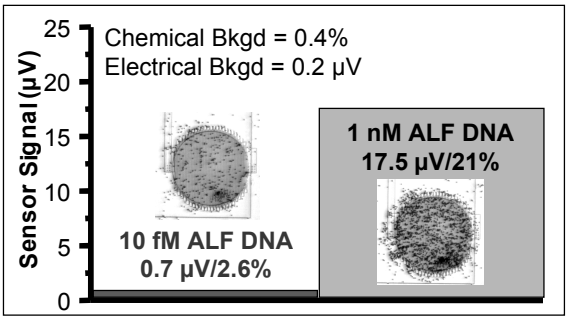


**Figure 3.** BARC III single-sensor assay results showing Anthrax lethal factor DNA detection for 10 fM and 1 nM concentrations. The complete assay required about 40 minutes. Both the sensor signal and optical micrographs of the sensor are shown. The percent of the sensor covered by beads in each case is also indicated.

## 4. Conclusions

Through the synergism of various macro and micro components, a complete and effective non-optical system for the analysis of DNA samples has been demonstrated. The use of state-of-the-art solid-state GMR sensors, non-fouling surface and assay chemistries, and a specially designed fluidics system has all contributed to the high detection sensitivity achieved by the BARC instrument.

## Acknowledgements

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